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IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

THE CENTRAL INSTITUTE FOR EXPERIMENTAL ANIMALS, a Japanese corporation, Plaintiff, v. THE JACKSON LABORATORY, a Maine corporation, Defendant.	No. C-08-05568 RMW ORDER CONSTRUING CLAIMS OF UNITED STATES PATENT NOS. 7,145,055 AND 5,912,173 **[Re Docket Nos. 99, 100]**

Plaintiff, The Central Institute for Experimental Animals ("CIEA"), brings this suit against defendant, The Jackson Laboratory ("Jackson"), alleging infringement of United States Patent No. 7,145,055 ("'055 Patent"). Jackson brings a counterclaim against CIEA, alleging infringement of United States Patent No. 5,912,173 ("'173 Patent"). The parties seek construction of claims in the '055 Patent and the '173 Patent. The court held a tutorial and claim construction hearing on February 2, 2010. After consideration of the claims, specification, prosecution history, and other relevant evidence, and after hearing the arguments of the parties, the court construes the disputed language of the patents-in-suit as set forth below.

I. ANALYSIS

A. The '055 Patent

The '055 Patent claims a method of producing a mouse with enhanced engraftment properties by backcrossing two strains of mice (as well as the mouse produced by this method and the use of

the mouse). Engraftment is a process in which the cells of one animal, such as a human, are transplanted into another animal, such as a mouse. Researchers have tried to improve the engraftment properties of mice (by reducing the potential of the host's immune system rejecting the transplanted cells) in order to study human diseases through the use of mice models. Backcrossing is a process of mating two animals so that the offspring have a genetic identity that is closer to the genetic identity of a selected parent. Typically, this involves breeding two mice with different genetic backgrounds, then breeding the offspring with the selected parent (or a mouse genetically similar to the selected parent). Each time the mouse is backcrossed in this way, the percentage of the genetic material of the selected parent that is present in the mouse increases.

Claim 1 of the '055 Patent claims the following:

> A mouse produced by a method comprising backcrossing a mouse B with a **mouse A**, wherein said **mouse A** is a mouse obtained by backcrossing a C.B.-17-scid mouse with an **NOD/Shi mouse**, and wherein said mouse B is an interleukin 2 receptor γ chain gene knockout mouse, wherein said mouse produced by the method does not express the interleukin 2 receptor γ chain, has enhanced engraftment capacity of heterologous cells relative to a **NOD/Shi-scid mouse**, has neither functional T-cells nor functional B-cells, exhibits reduced **macrophage function** relative to a **NOD/shi-scid mouse**, exhibits no NK cells or NK cell activity, and exhibits reduced dendritic function relative to a **NOD/Shi-scid mouse**.

'055 Patent 35:10-22 (emphasis added). The parties seek construction of the terms: "NOD/Shi mouse," "NOD/Shi-scid mouse" (or "mouse A"), and "macrophage function."

1. "NOD/Shi Mouse" and "NOD/Shi-scid Mouse"

The parties' proposed constructions are as follows:

CLAIM LANGUAGE	CIEA'S PROPOSED CONSTRUCTION	JACKSON'S PROPOSED CONSTRUCTION
"NOD/Shi mouse"	A NOD mouse, i.e. a mouse with a NOD strain background.	A non-obese diabetic mouse from the original NOD mouse colony created by Dr. Susumu Makino at Shionogi Research Laboratories, or a mouse separated from that colony by less than 20 generations. NOD/Shi mice are commercially available from CLEA JAPAN, INC.

CLAIM LANGUAGE	CIEA'S PROPOSED CONSTRUCTION	JACKSON'S PROPOSED CONSTRUCTION
"mouse A" and "NOD/Shi-scid mouse"	A NOD/scid mouse, i.e. a mouse with a NOD/scid strain background.	A mouse strain produced by multiple backcross generations of a C.B.-17 scid mouse with a non-obese diabetic mouse from the original NOD mouse colony created by Dr. Susumu Makino at Shionogi Research Laboratories, or with a mouse separated from that colony by less than 20 generations. NOD/Shi-scid mice are commercially available from CLEA JAPAN, INC.

The parties agree that "mouse A" refers to a "NOD/Shi-scid mouse" and thus the two terms should be construed identically. The parties also agree on the following: (1) "NOD" refers to non-obese diabetic mice; (2) "Shi" is a laboratory code for the Shionogi Research Laboratory in Japan; and (3) "scid" refers to the mouse's severe combined immunodeficiency background. What the parties dispute is the meaning and significance of "Shi" as used in "NOD/Shi mouse" and "NOD/Shi-scid mouse."

CIEA contends that the "Shi" in "NOD/Shi mouse" and "NOD/Shi-scid mouse" merely refers to the fact that the mouse can be traced back to the NOD/Shi colony (the NOD mouse colony created by Dr. Susumu Makino at Shionogi Research Laboratories), regardless of the number of generations the mouse has been separated from that colony. Since all NOD mice can be traced back to the NOD/Shi colony, CIEA seeks a construction that equates "NOD/Shi mouse" with "NOD mouse" and equates "NOD/Shi-scid mouse" with "NOD-scid mouse." Jackson, on the other hand, argues that the "Shi" in "NOD/Shi mouse" and "NOD/Shi-scid mouse" refers to a specific mouse strain, including only mice that have not been separated from the NOD/Shi colony or have been separated from that colony by less than twenty generations. Under Jackson's proposed construction, NOD/Shi mice are a subset of NOD mice and are not the same. Likewise, NOD/Shi-scid mice are only a subset of NOD-scid mice and are not identical.

Claim terms are generally construed to mean what a person of ordinary skill in the art at the time of the invention would have understood the terms to mean. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005). When the meaning of a claim term, as understood by persons of

ordinary skill in the art, is not immediately apparent, courts are to look to sources available to the public to determine what the disputed claim language means. *Id.* at 1314. These sources include "the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." *Id.* (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004)).

The court thus begins by looking at the words of the claims themselves. *Vitronics Corp. v. Conceptronic*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). The claims use the term "NOD/Shi mouse" rather than "NOD mouse." As explained above, adopting CIEA's proposed construction and interpreting "NOD/Shi mouse" to include any mouse that can be traced back to the NOD/Shi colony would equate "NOD/Shi mouse" with "NOD mouse" and read "Shi" out of the claims. Because a "claim construction that gives meaning to all the terms of the claim is preferred over one that does not do so," *Merck & Co., Inc. v. Teva Pharmaceuticals USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005), the claim language supports Jackson's contention that "NOD/Shi mouse" is not the same as "NOD mouse." *See also Phillips*, 415 F.3d at 1314 (claim language "steel baffles" "strongly implies that the term 'baffles' does not inherently mean objects made of steel").

The specification provides further evidence that "NOD/Shi mouse" does not include all NOD mice (and that "NOD/Shi-scid mouse" does not include all NOD-scid mice). Claims are read in light of the specification, which is the "single best guide to the meaning of the disputed term." *Phillips*, 415 F.3d at 1315. At times, the applicant uses the clearly generic term "NOD-scid" in the patent rather than "NOD/Shi-scid." *See, e.g.*, '055 Patent Fig. 1; '055 Patent 9:4-7 ("Fig. 4 shows . . . a comparative test between the NOG mouse and a β2 microglobulin deficient *NOD-SCID mouse* (NOD/LtSz-scid, β 2 m null mouse).") (emphasis added). The fact that the patent uses both the term "NOD/Shi-scid" and the term "NOD-scid" suggests that the two phrases do not refer to the same mouse. Moreover, since the patent contains the clearly generic term "NOD-scid," the inventor clearly was aware of this generic term and could have chosen to use "NOD-scid" rather than "NOD/Shi-scid" when drafting the claims.

In addition, the specification states: "Above all, an NOD/Shi-scid mouse and an NOD/LtSz-scid mouse which exhibit multifunctional immunodeficiency . . . are the most noteworthy laboratory animals suitable for engraftment of heterologous cells." '055 Patent 1:32-38. By referring separately to NOD/Shi-scid mice and NOD/LtSz-scid mice, this statement acknowledges a difference between the two and provides further evidence that "NOD/Shi-scid" is not the same as "NOD-scid." After all, if "NOD/Shi-scid mouse" were construed to mean NOD-scid mouse, any reference to NOD/Shi-scid mice would include NOD/LtSz-scid mice. Under this construction, it would be redundant to say both NOD/Shi-scid mice and NOD/LtSz-scid mice are "the most noteworthy laboratory animals" since NOD/LtSz-scid mice would already be included as a subset of NOD/Shi-scid.[1]

The language in the prosecution history upon which CIEA relies demonstrates that the patentee recognized (and that a person of ordinary skill in the art would have recognized) that the term "NOD/Shi-scid mouse" did not include all NOD-scid mice. For example, the patentee wrote:

> As shown in Figure 1 and the description[] in the section "Similarity of multiple immunological impairments between NOD-Shi-scid and Nod/LtSz-scid mice,["] the immunological properties of these two mice were the same. It was known that the NOD-LtSz-scid mice were a sub-strain[] of NOD-Shi-scid mice. It can, therefore, be said that the NOD-LtSz-scid mice are substantially the same strain [as] the NOD-Shi-scid mice.

Decl. of Ronald M. Daignault in support of CIEA's Opening Cl. Construction Br. ("Daignault Decl.") Ex. 2 (CIEA-0003199). Though this passage stresses the similarities in the immunological properties of NOD/Shi-scid mice and NOD/LtSz-scid mice, by comparing the two, it implicitly acknowledges that the terms "NOD/Shi-scid" and "NOD/LtSz-scid" refer to distinct types of mice. After all, if "NOD/Shi-scid mouse" were construed to include all NOD-scid mice, this passage would be nonsensical. One cannot compare the immunological properties between NOD-scid mice and NOD/LtSz-scid mice because NOD/LtSz-scid mice are a subset of NOD-scid mice. Nor does it make any sense to say that NOD/LtSz-scid mice are substantially the same strain as NOD-scid

[1] To illustrate this point, consider the following sentence: "Apples and oranges are the tastiest foods available." This sentence makes sense because apples and oranges are two distinct types of food. One would not say, "Fruit and oranges are the tastiest foods available" because the fact that oranges are a subset of fruit makes the phrase "and oranges" redundant.

mice.[2] As discussed above, the language of the claims themselves, the specification, and the prosecution history make clear that "NOD/Shi mouse" does *not* include all NOD mice (and that "NOD/Shi-scid mouse" does *not* include all NOD-scid mouse). Unfortunately, these sources do not provide the court with much information as to what mice *are* included within the meaning of the disputed terms. However, the patent cites and incorporates various scientific publications which shed some light on the meaning of the disputed terms. Prior art cited in the patent constitute intrinsic evidence to be considered during claim construction. *Arthur A. Collins, Inc. v. Northern Telecom Ltd.*, 216 F.3d 1042, 1045 (Fed Cir. 2000). "When prior art that sheds light on the meaning of a term is cited by the patentee, it can have particular value as a guide to the proper construction of the term, because it may indicate not only the meaning of the term to persons skilled in the art, but also that the patentee intended to adopt that meaning." *Id.*

The scientific publications cited in the '055 Patent provide additional confirmation that "NOD/Shi mouse" is not equivalent to "NOD mouse" (and that "NOD/Shi-scid mouse" is not equivalent to "NOD-scid mouse") and provide insight as to what mice are included within the scope of the disputed terms. For example, the patent cites "NOD/SCID/γc^{null} mouse: an excellent recipient mouse model for engraftment of human cells," an article in *BLOOD* that was authored by six of the inventors. This article uses the term "NOD" (not "NOD/Shi") when referring to all NOD mice and compares NOD/Shi-scid mice to NOD/LtSz-scid mice. Decl. of Chelsea A. Loughran in support of Jackson's Responsive Cl. Construction Br. for the '055 Patent ("Loughran Decl.") Ex. G. It also states: "*NOD/Shi* with different genetic backgrounds used for the generation of NOD/Shi-scid mouse *is an original strain maintained by Dr. Makino*." *Id.* (emphasis added). This indicates not only that a person of ordinary skill in the art would understand that "NOD/Shi mouse" refers to mice from the original NOD mouse colony created by Dr. Susumu Makino (and does not refer to all substrains of mice that descended from this colony), but also that the patentee intended to adopt this meaning. *Arthur A. Collins, Inc.*, 216 F.3d at 1045.

[2] To continue the earlier fruit example, this would be like saying oranges are substantially the same as fruit.

Though courts are to look first to intrinsic evidence, they may also rely on expert testimony when it establishes that a term has a particular meaning in the pertinent field, so long as it does not contradict the claim language itself, the specification, and the prosecution history. *Phillips*, 415 F.3d at 1318. Extrinsic evidence, such as expert testimony, is generally less reliable than intrinsic evidence. Nonetheless, "because extrinsic evidence can help educate the court regarding the field of the invention and can help the court determine what a person of ordinary skill in the art would understand claim terms to mean, it is permissible for the district court in its sound discretion to admit and use such evidence." *Id.* at 1319. The court therefore considers the expert testimony of Dr. Janan T. Eppig in determining what a person of ordinary skill in the art would understand the disputed claim terms to mean.

Dr. Eppig, the chairperson of the International Committee on Standardized Genetic Nomenclature in Mice, testified regarding inbred mouse strains, mouse substrains, and rules for mouse nomenclature. In order to reliably reproduce experiments involving mice, researchers strive to maintain populations of mice with a homogenous genetic makeup. Decl. of Dr. Janan T. Eppig in support of Jackson's Proposed Claim Construction ("Eppig Decl.") ¶ 27. To create a mice colony with a homogenous genetic makeup, researchers breed mice with siblings for twenty or more consecutive generations, creating what is known as an inbred mouse strain. *Id.* at ¶¶ 28-29. If mice from the inbred colony are reproductively separated from the colony for more than twenty generations, it is likely that there will be genetic drift, meaning that the genetic makeup of the mice in the new colony will no longer be the same as the genetic makeup of mice in the original inbred colony. *Id.* at ¶ 30. The mice in the new colony constitute a new mouse substrain, and the rules for mouse nomenclature require re-designating the new colony as such. *Id.*

In light of the rules of mouse nomenclature, a person of ordinary skill in the art would understand "NOD/Shi mouse" to refer to a mouse that had not been reproductively separated from the inbred NOD mouse colony created by Dr. Susumu Makino at Shionogi Research Laboratories or had been separated by twenty or fewer generations. Once mice have been reproductively separated from this inbred colony for more than twenty generations, they would constitute a new mouse substrain with a distinct name, such as the NOD/LtSz substrain. *Id.* at ¶ 31.

Extrinsic evidence, such as expert testimony, cannot be used to contradict intrinsic evidence, including the specification. *Vitrionics*, 90 F.3d at 1584. The specification clearly states that a NOD/Shi mouse is "commercially available from CLEA JAPAN, INC." '055 Patent 4:29-30. Consequently, the court may not construe the disputed terms using extrinsic evidence about the rules of mouse nomenclature if these rules contradict the specification's express declaration that NOD/Shi mice are commercially available from CLEA JAPAN, INC. Because CLEA JAPAN, INC. ("CLEA") is the commercial arm of CIEA, CIEA possesses information regarding what kinds of mice were commercially available from CLEA at the time of the invention. However, CIEA has failed to come forth with any evidence that NOD/Shi mice (construed according to the rules of mouse nomenclature) were not commercially available from CLEA at the time of the invention.

If "NOD/Shi mouse" were construed according to the rules of mouse nomenclature, there are three possible scenarios under which NOD/Shi mice could have been commercially available from CLEA at the time of the invention: (1) the entire colony of NOD/Shi mice had been moved from the Shionogi Laboratory to CLEA; (2) the CLEA colony was periodically repopulated with NOD/Shi mice from Shionogi Laboratory; or (3) at the time of the invention, there had not yet been more than twenty generations of reproductive separation between the NOD/Shi mice that were moved to CLEA and the colony of NOD/Shi mice at Shionogi Laboratory. In the absence of any evidence to the contrary, any of these scenarios are possible, though only the second scenario seems particularly plausible. Jackson presented evidence that CIEA has, in the past, entered into at least one license agreement that required replenishing of its mice colony once every ten generations.[3] Thus, Jackson has shown how NOD/Shi mice (construed according to the rules of mouse nomenclature) could have been commercially available from CLEA, as required by the patent specification, and CIEA has failed to provide any evidence to the contrary. Therefore, the court finds no basis for excluding Dr. Eppig's testimony regarding the rules for mouse nomenclature from its consideration when construing the disputed terms.

[3] CIEA objected to the admission of this license agreement because Jackson had not produced it before the hearing. Jackson represented that it just recently obtained the document. Based upon that representation and the fact that it is a CIEA agreement, the court has considered it.

The issues faced in construing "NOD/Shi mouse" and "NOD/Shi-scid mouse" are similar to those addressed in *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339 (Fed. Cir. 2003). In *Boehringer*, the Federal Circuit considered a patent that was directed to a process for growing and isolating a pig virus known as PRRS. 320 F.3d at 1343. The Boehringer scientists who invented the method had deposited a sample of the virus with the American Type Culture Collection (ATCC), which had assigned it deposit number VR-2332. *Id.* The patent claimed "[a] method of growing and isolating swine infertility and respiratory syndrome virus, ATCC-VR2332." *Id.* at 1344. The district court rejected Boehringer's argument that "ATCC-VR2332" should be construed as a generic term for all PRRS viruses and held that it was limited to the specific strain of PRRS deposited with the ATCC. *Id.* at 1347-48. The Federal Circuit upheld the district court's claim construction because:

> Boehringer chose to claim its virus using the term "ATCC-VR2332," a term on its face referring to a particular ATCC deposit. Boehringer did not use the broader term "PRRS virus," nor did Boehringer attempt to claim the virus in terms of the more general functional and structural properties disclosed by the specification. Boehringer did not choose to define the term "ATCC-VR2332" in the specification, nor did Boehringer state that ATCC-VR2332 was a "generic" or "prototype" virus, nor did Boehringer assert that viruses related to but not identical to the isolated strain were within the scope of the invention. These choices must be held against it.

Id. at 1348. Similarly, the inventors in this case chose to draft claims using the term "NOD/Shi mouse" and "NOD/Shi-scid mouse," rather than using the broader terms "NOD mouse" and "NOD-scid mouse." Though CIEA now points to similarities in the genetic background and immunological properties of NOD/Shi-scid mice and NOD/LtSz-scid mice, the inventors did not claim the mouse in terms of more general genetic or immunological properties. The inventors did not choose to define the disputed terms in the specification, nor did they state that "NOD/Shi mouse" and "NOD/Shi-scid mouse" were generic terms referring to NOD mice and NOD-scid mice, nor did they assert that mice related to but not identical to the identified mouse substrain were within the scope of the invention. Accordingly, these choices must be held against the inventors.

The court therefore construes "NOD/Shi mouse" to mean a non-obese diabetic mouse that: (1) has not been reproductively separated from the NOD mouse colony created by Dr. Susumu Makino at Shionogi Research Laboratories or (2) has been reproductively separated from that colony

by 20 or fewer generations.[4] The court declines to include the statement that "NOD/Shi mice are commercially available from CLEA JAPAN, INC." in the construction because the court finds that including such a statement would likely be more confusing than clarifying. Though the specification states that NOD/Shi mice are commercially available from CLEA, this does not mean that NOD/Shi mice must still be commercially available from CLEA today; rather it only requires that NOD/Shi mice were commercially available from CLEA at the time of the invention.

2. "Macrophage Function"

Claim 1 of the '055 Patent claims a mouse that "exhibits reduced macrophage function relative to a NOD/Shi-scid mouse." '055 Patent 35:19-20. A macrophage is a type of white blood cell. The parties agree that macrophages perform two primary functions: (1) ingesting foreign particles and (2) producing chemicals called cytokines, which stimulate other parts of the immune system to react to foreign pathogens. Pursuant to the parties' stipulation during the claim construction hearing, the court construes "macrophage function" to mean the ability of macrophage cells to ingest foreign particles and to produce cytokines.

B. The '173 Patent

The '173 Patent is directed to the isolation, sequencing, and mutation of the IL-2Rγ gene in mice. This gene plays a key role in immune function. In humans, a defective or mutated IL-2Rγ gene causes a rare immunological disease called X-linked severe combined immunodeficiency ("XSCID"), which is commonly referred to as "bubble boy syndrome." The '173 Patent discloses a technique for creating a mouse with an IL-2Rγ deficiency that mimics human XSCID.

The first step in this technique involves inserting foreign DNA into the genome of a target mouse embryonic stem cell. The foreign DNA is inserted by a vector, and the cell's normal IL-2Rγ gene is modified by a process known as homologous recombination. The resulting cell with a mutated IL-2Rγ gene is called a transgenic cell. Transgenic embryonic stem cells are then inserted into a mass of normal embryonic stem cells (called a blastocyst), and this mass is implanted into a

[4] Though Jackson's proposed construction uses "less than 20 generations" of separation, Dr. Eppig's expert testimony regarding the rules of mouse nomenclature establishes that substrain designation occurs when there is *more than* 20 generations of separation. Eppig Decl. ¶ 30. For this reason, the court adopts a construction based on 20 or fewer generations of separation, rather than less than 20 generations of separation.

female foster mouse. Inside the foster mouse, the cells grow, divide, and differentiate, eventually forming a fetus.[5] The cells in the fetus formed from the transgenic embryonic stem cells will have the IL-2Rγ mutation, while those formed from the original normal cell mass will not. By breeding these offspring mice, one can obtain mice with an IL-2Rγ deficiency that mimics human XSCID.

The '173 Patent claims certain mouse cells having a mutated IL-2Rγ gene as well as certain vectors and methods for causing an IL-2Rγ deficiency in mice. The parties seek construction of the terms "vector," "murine embryonic stem cell," "transfected mouse cell," "IL-2Rγ deficient mouse cell," and "transgenic mouse cell." The parties' proposed constructions are as follows:

CLAIM LANGUAGE	CIEA'S PROPOSED CONSTRUCTION	JACKSON'S PROPOSED CONSTRUCTION
"vector"	A DNA agent (usually a virus or plasmid) generally used in a cloning process or to transmit genetic material to a cell or organism **that is a stand-alone product and is purchased or licensed as a stand-alone product separate and apart from a mouse**.	A DNA agent (usually a virus or plasmid) generally used in a cloning process or to transmit genetic material to a cell or organism.
"murine embryonic stem cell"	A mouse embryonic stem cell **that is a stand-alone product and is purchased or licensed as a stand-alone product separate and apart from a mouse.**	A mouse embryonic stem cell.
"transfected mouse cell"	A mouse cell into which foreign DNA has been introduced **that is a stand-alone product and is purchased or licensed as a stand-alone product separate and apart from a mouse.**	A mouse cell into which foreign DNA has been introduced**.**
"IL-2Rγ deficient mouse cell	A mouse cell bearing a deficiency in the IL-2Rγ gene **that is a stand-alone product and is purchased or licensed as a stand-alone product separate and apart from a mouse.**	A mouse cell bearing a deficiency in the IL-2Rγ gene.
"transgenic mouse cell"	A mouse cell with a mutated gene sequence **that is a stand-alone product and is purchased or licensed as a stand-alone product separate and apart from a mouse.**	A mouse cell with a mutated gene sequence.

[5] Differentiation is a process where embryonic stem cells becomes more specialized, turning into different types of cells, such as a heart cell or a brain cell.

As shown above, the parties' constructions are identical, except that CIEA's proposed construction includes the limitation that the vector or cell is "a stand-alone product and is purchased or licensed as a stand-alone product separate and apart from a mouse." Based on CIEA's briefing and its argument at the claim construction hearing, CIEA appears to seek a construction that includes only *in vitro* cells or vectors (cells or vectors in a petri dish, outside of a mouse) and excludes all *in vivo* cells or vectors (cells or vectors inside a mouse). Jackson contends that no such *in vitro* limitation should be adopted.

1. "Vector"

It is undisputed that the term "vector" refers to a DNA agent (usually a virus or plasmid) generally used in a cloning process or to transmit genetic material to a cell or organism. CIEA contends that vectors can only exist *in vitro* and cannot exist within mice, while Jackson argues that vectors continue to exist in mice, even after accomplishing their purpose. However, Jackson conceded at the claim construction hearing that a vector is "the *vehicle* that you use to disrupt the gene." *See also* Jackson's Opening Cl. Construction Br. for the '173 Patent at 13 ("vectors are *vehicles* into which one can insert a gene or a sequence of DNA") (emphasis added). Even when the vector is a replacement construct (as described in the '173 Patent), once it has been used, the vector no longer exists. When a replacement construct is used, part of the gene sequence in the vector is retained in the cell, but there is no longer a vehicle for cloning or transmitting genetic material. '173 Patent 3:51-59. Accordingly, the court construes "vector" to mean a DNA agent (usually a virus or plasmid) generally used in a cloning process or to transmit genetic material to a cell or organism. Vectors do not continue to exist after they have been used in a cell or organism.

2. "Murine Embryonic Stem Cell"

Both parties agree that the term "murine embryonic stem cell" refers to a mouse embryonic stem cell. As discussed above, the '173 Patent describes a process for creating a mouse with an IL-2Rγ deficiency, which involves inserting transgenic mouse embryonic stem cells into a mass of normal embryonic stem cells and then implanting this mass into a female foster mouse. '173 Patent 4:47-49. CIEA explained in its briefs and at the claim construction hearing that with respect to this term, it does not seek a limitation that excludes all *in vivo* cells. CIEA seeks a construction that

includes embryonic stem cells after they have been implanted in a mouse so long as they have not yet undergone cell differentiation. CIEA's Opp'n for the '173 Patent at 2 n.2. In other words, CIEA seeks to exclude *in vivo* cells only after they have undergone cell differentiation.

Once an embryonic stem cell has undergone cell differentiation, it becomes a specialized cell and is no longer referred to as an embryonic stem cell. Thus, by definition, an embryonic stem cell is a non-differentiated cell, and Jackson's proposed construction satisfies the limitation CIEA seeks (to exclude differentiated cells). To make this clear, the court adopts Jackson's construction but adds the clarification that all embryonic stem cells are non-differentiated cells.

3. "Transfected Mouse Cell," "IL-2Rγ Deficient Mouse Cell," and "Transgenic Mouse Cell"

CIEA contends that the plain language of the '173 Patent supports an *in vivo* limitation. CIEA's argument appears to be that because the claims use the word "cell" rather than "mouse," the patent claims only *in vitro* cells and not cells inside mice. While CIEA is undoubtedly correct that the patent claims cells, not mice, this does not support the leap in logic that one must make to then conclude that the cells claimed are limited to cells outside of a mouse and cannot include cells within a mouse.

Next, CIEA argues that the court should construe the disputed terms as having an *in vitro* limitation in order to preserve claim validity. Without an *in vitro* limitation, CIEA alleges, the claims would include naturally-occurring cells and therefore be invalid under 35 U.S.C. § 101. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (holding that naturally occurring phenomena are not patentable). CIEA claims that "SCID could occur in non-genetically engineered mice" but provides no evidence that the IL-2Rγ gene mutation has ever occurred naturally in mice. CIEA's Opp'n for the '173 Patent at 7. Jackson's expert, Dr. Leonard Shultz, testified, "such a mutation has never, to my knowledge, occurred spontaneously in mice." Decl. of Dr. Leonard D. Shultz in support of Jackson's Cl. Construction Reply Br. for the '173 Patent ("Shultz Decl.") ¶ 12. Moreover, Dr. Shultz testified that "transgenic" and "transfected" refer to genetically engineered cells that do not occur in nature. Shultz Decl. ¶ 21.

It is undisputed that the terms "transfected mouse cell," "IL-2Rγ deficient mouse cell," and "transgenic mouse cell" refer to genetically engineered cells, not naturally occurring cells.

Construing these terms as having this limitation is consistent with the language in the patent and also maintains claim validity. Therefore, the court construes these terms as limited to genetically engineered cells.

Finally, CIEA points to the prosecution history of the '173 Patent as supporting its contention that an *in vivo* limitation should be adopted. The applicant had tried to claim a transgenic mouse, the claim was rejected by the Examiner, and the applicant eventually acquiesced to this rejection by canceling the claim for a transgenic mouse. In light of this prosecution history, there can be no doubt that the patent does not claim transgenic mice. However, as discussed above, this does not support the leap in logic that one must make to then conclude that the cells claimed in the patent are limited to cells outside of a mouse and cannot include cells within a mouse. CIEA has failed to point to any language in the prosecution history suggesting that the Examiner only intended to allow the applicant to claim *in vivo* cells. Limitations of claim scope based on the prosecution history require a "clear and unmistakable disavowal" of claim scope. *Univ. of Pittsburgh of the Commonwealth Sys. of Higher Educ. v. Hedrick*, 583 F.3d 1290, 1297 (Fed. Cir. 2009). The court finds no such "clear and unmistakable disavowal" here. In the absence of any evidence in the patent or the prosecution history that the claimed cells are limited to *in vitro* cells, the court declines to adopt an *in vitro* limitation. The court therefore adopts Jackson's proposed constructions, with the addition of the phrase "genetically engineered" to make this limitation clear.

II. ORDER

For the foregoing reasons, the court construes the disputed claim language as follows:

'055 PATENT CLAIM LANGUAGE	CONSTRUCTION
"NOD/Shi mouse"	A non-obese diabetic mouse that: (1) has not been reproductively separated from the NOD mouse colony created by Dr. Susumu Makino at Shionogi Research Laboratories or (2) has been reproductively separated from that colony by 20 or fewer generations.
"mouse A" and "NOD/Shi-scid mouse"	A mouse strain produced by multiple backcross generations of a C.B.-17 scid mouse with a NOD/Shi mouse.
"macrophage function"	The ability of macrophage cells to ingest foreign particles and to produce cytokines.

'173 PATENT CLAIM LANGUAGE	CONSTRUCTION
"vector"	A DNA agent (usually a virus or plasmid) generally used in a cloning process or to transmit genetic material to a cell or organism. Vectors do not continue to exist after they have been used in a cell or organism.
"murine embryonic stem cell"	A mouse embryonic stem cell. All embryonic stem cells are non-differentiated cells.
"transfected mouse cell"	A genetically engineered mouse cell into which foreign DNA has been introduced**.**
"IL-2Rγ deficient mouse cell	A genetically engineered mouse cell bearing a deficiency in the IL-2Rγ gene.
"transgenic mouse cell"	A genetically engineered mouse cell with a mutated gene sequence.

DATED: 2/8/10

Ronald M. Whyte

RONALD M. WHYTE
United States District Judge

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Dated: 2/8/10

CCL
Chambers of Judge Whyte